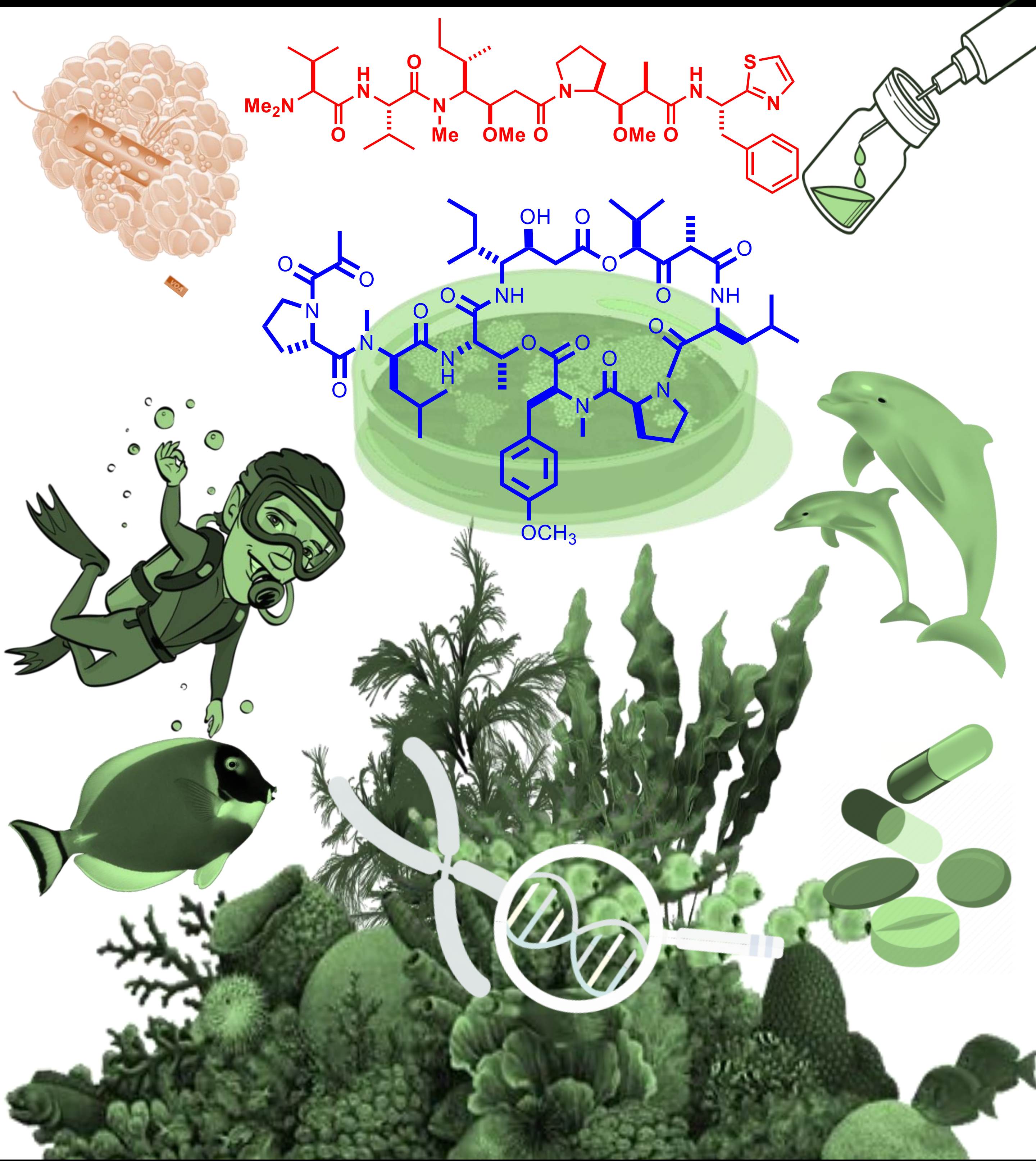
Marine Drugs

2021 – 2022 {Lecture 7}



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IV. Marine Chemical Ecology

Science deals with the chemical interactions between living marine organisms with each other and with the environment {It guides us as pharmacists to discover new drugs}

1. Puffer Fish, *Pseudoalteromonas* and Tetrodotoxin

Tetrodotoxin was isolated from Puffer fish. The actual producer is certain symbiotic bacteria {*Pseudoalteromonas* gram –ve M.O}. Tetrodotoxin acts as a very strong sodium channel blocker. It is converted into a pain killer medicine Halneuron® by WEX Pharmaceuticals Canada. It is 3000 times more active than morphine as pain killer.

2. Cone Snail, Fish and ω-Conotoxin

Snail called Conus magus in Philippine attacks fish by injecting mixture of cyclic peptides into fish, paralyzing them then predate on them. The major bioactive polypeptide was ω-conotoxin block voltage-gated calcium channels in neurons. The synthetic analogue of ω-conotoxin {Ziconotide - Prialt®} was produced and marketed now in year 2004. It is used to treat severe chronic pain in people who cannot use or do not respond to standard pain-relieving medications. It is 1000 times more active than morphine as pain killer.

3. *Dolabella auricularia*, Cyanobacteria and Dolastatin 10

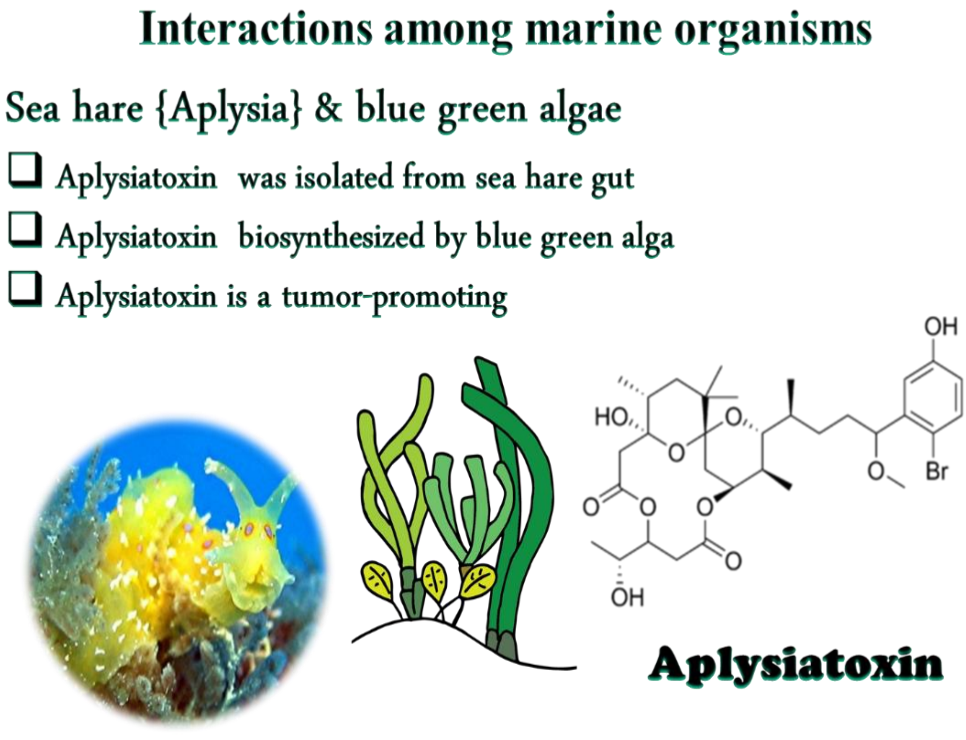
Dolastatin 10 was isolated for the first time from *Dolabella auricularia*. Evolution scientists said that nudibranchs were developed from snails losing their shells, starting produce toxic compounds as deference mechanism against enemies. Dolastatins, including dolastatin 10 recently isolated from blue green alga {*Moorea producens*}. Blue green algae produce these compounds as anti-deterrent against *Dolabella auricularia*. Brentuximab, a very strong and selective drug used for lymphoma was inspired from Dolastatin 10.

Cyanobacteria or Blue green algae

Scientists debate about the nomenclature of Cyanobacteria to be Cyanobacteria or to be blue green algae? Some scientists named them Cyanobacteria as the cell wall consisting of peptidoglycans {like bacteria} and a mixture of pigments. Other scientists named them blue green algae as they contain chlorophyll {green pigments} and Phycobillin {Blue pigments}. Blue green algae carry out photosynthesis using chlorophyll A.

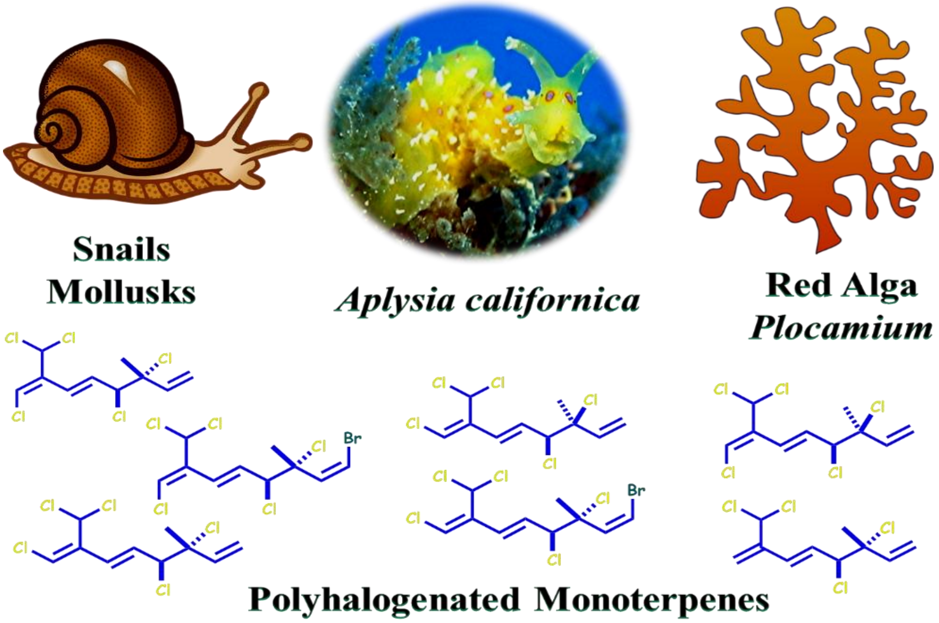
4. Sea Hare, Blue Green Algae and Aplysiatoxin

Aplysiatoxin isolated from the gut of *Stylocheilus longicauda*, a sea hare, then from the blue green algae. Blue green algae produce Aplysiatoxin as anti-predator against sea hare. Scientists confirmed the true producer by isolation of the gene cluster from the Cyanobacteria. Aplysiatoxin in small dose activates protein kinase C {PKC} leading to cell death. Aplysiatoxin is a tumor promoter in large dose, and in small dose it is anti-tumor {cytotoxic for cancer cells}.



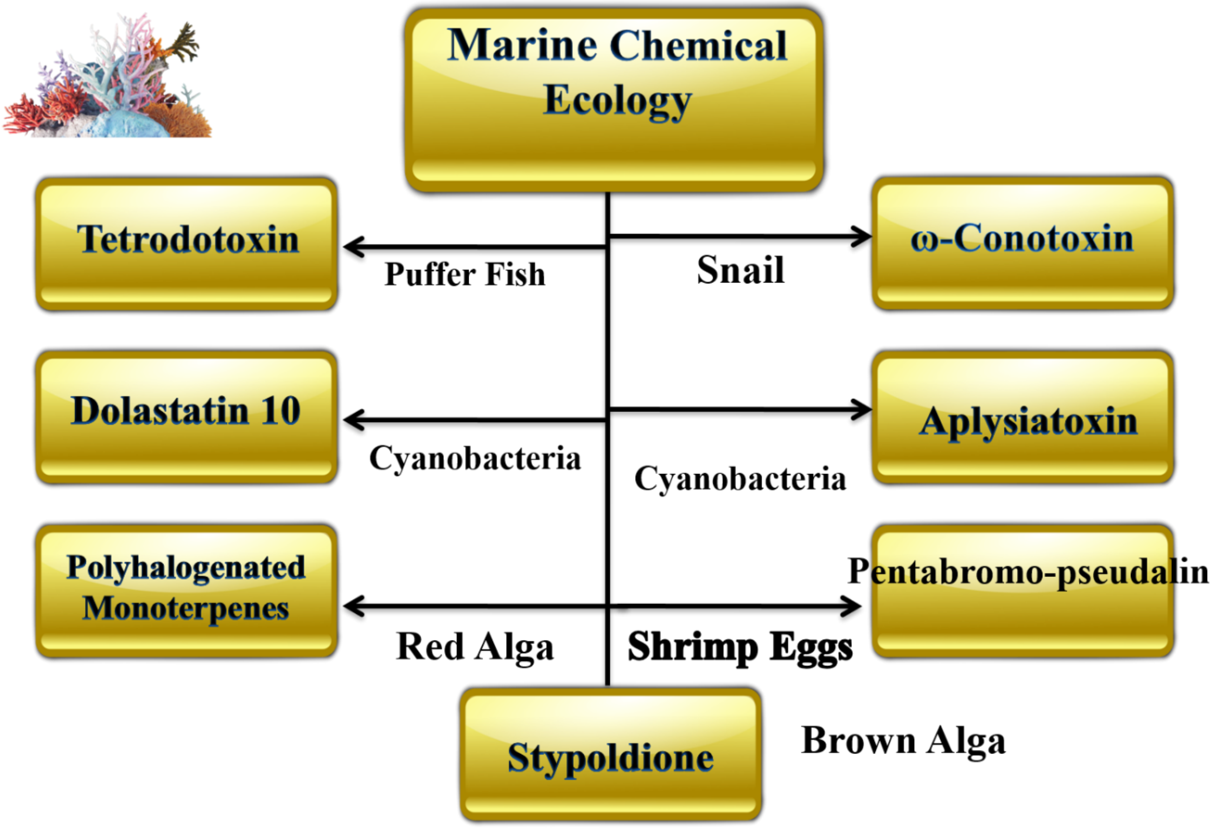
5. Nudibranchs, Red Algae and Polyhalogenated Monoterpenes

Poly-halogenated monoterpene compounds were isolated from the gut of certain nudibranchs {*Phyllidia coelestis*}. Polyhalogenated monoterpene compounds were recently isolated from the red alga "*Plocamium cartilagenum*". Red algae produce these compounds as anti-deterrent against nudibranchs. Polyalogenated monoterpene compounds showed strong cytotoxicity {5 times active} than taxol against breast cancer cell lines.



6. Brine Shrimp Eggs, Alteromonas and Fungi

Brine shrimp eggs hatch in ocean water by 80% in the normal environmental conditions. when washed by penicillin then leaving them in ocean water, this results in 0% hatching. washing eggs with penicillin then adding the gm-ve rods micro-organisms extract named *Altermonas* with ocean water, 60% hatching was obtained. Bacteria named *Altermonas* and some fungi were grown on the microbial culture of brine shrimp eggs. Bacteria is killing the fungi and eggs hatch. In absence of *Altermonas* bacteria, fungi will infect Brine Shrimp eggs and they will not hatch. a compound named Penta Bromo-pseudalin with very high anti-fungal activity in-vitro was isolated from *Altermonas*.

7. *Stypopodium*, Snail killing Activity and Stypoldione

Snails are not feeding on the brown alga *Stypopodium zonale*. The isolated compound stypoldione {Diterpenoid} was found to have ichtyotoxic activity = killing snails}. Stypoldione has sodium channel blocking activity {Neurotoxin}. It can be used as a drug lead in treatment of pain and convulsion resulting from epilepsy.